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Dr. Kodishala et al reply

To the Editor:

We thank Wang and colleagues[1] for their earnest interest in our recent paper, which evaluated the risk factors for dementia in an inception cohort of rheumatoid arthritis (RA).[2]

In their correspondence,[1] the authors point out a possibility of confounding by several factors, including age, sex, education, calendar year of RA incidence, and race, and suggest adjusting for these confounders. The results presented in the study[2] are already adjusted for age, sex, and calendar year of RA incidence. Although education and race have been previously associated with the risk of dementia in the general population,[3,4] these risk factors had no statistically significant association with dementia in our study.[2] We have acknowledged as a limitation that our population-based study includes predominantly White individuals, consistent with the racial distribution of the underlying population.

Wang et al suggest that chronic pain, a common symptom in RA, can be related to cognitive decline.[1] The association between pain and cognitive decline is complex. Although chronic pain can be associated with cognitive impairment,[5] assessment of pain in individuals with cognitive impairment is challenging because pain is a subjective symptom and is heavily dependent on self-reporting.[6] Disentangling the associations between pain and cognition was out of the scope of this study.[2] Instead, we report associations between a comprehensive list of RA disease-related risk factors including laboratory, radiographic, and clinical characteristics, and incident dementia.

Risk factors of interest including cardiovascular risk factors were evaluated at baseline and throughout the follow-up, and were appropriately modeled as time-dependent covariates, thus addressing the concern raised by Wang et al[1] about the change in the status of risk factors during the follow-up.

Wang et al[1] point out that single timepoint measures of inflammatory markers (erythrocyte sedimentation rate [ESR]) may not be reflective of the cumulative inflammatory burden of RA and using multiple timepoint measures of ESR can improve understanding of the association between systemic inflammation and dementia risk. We agree with these considerations. Although the study included associations between ESR at baseline and highest ESR in the first year of RA with the risk of incident dementia in RA, comprehensive analyses of the association between cumulative inflammatory marker measures and risk of dementia in RA are underway by our group.

Wang et al[1] point out that the study did not provide information on RA disease activity scores and dementia subtypes. These comments reiterate limitations that have been already acknowledged in the article.[2]

Wang et al[1] comment that "the homogeneous (eg, single racial/ethnic group) and small sample nature of this study limits its generalizability." In our population-based study,[2] sample size reflects the epidemiology of RA in the studied underlying population, which is predominantly White but includes approximately 10% of individuals of other races and ethnicities like Hispanic, Asian, African American, American Indian, and Native Hawaiian populations. Thus, the results are generalizable to populations with similar racial and ethnic distribution, although the generalizability to more diverse populations may be limited, as pointed out in the limitations.

Overall, we sincerely thank Wang and colleagues for their interest, time, and effort to bring forth these points of discussion through our study.

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The authors declare no conflict of interest relevant to this study.

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